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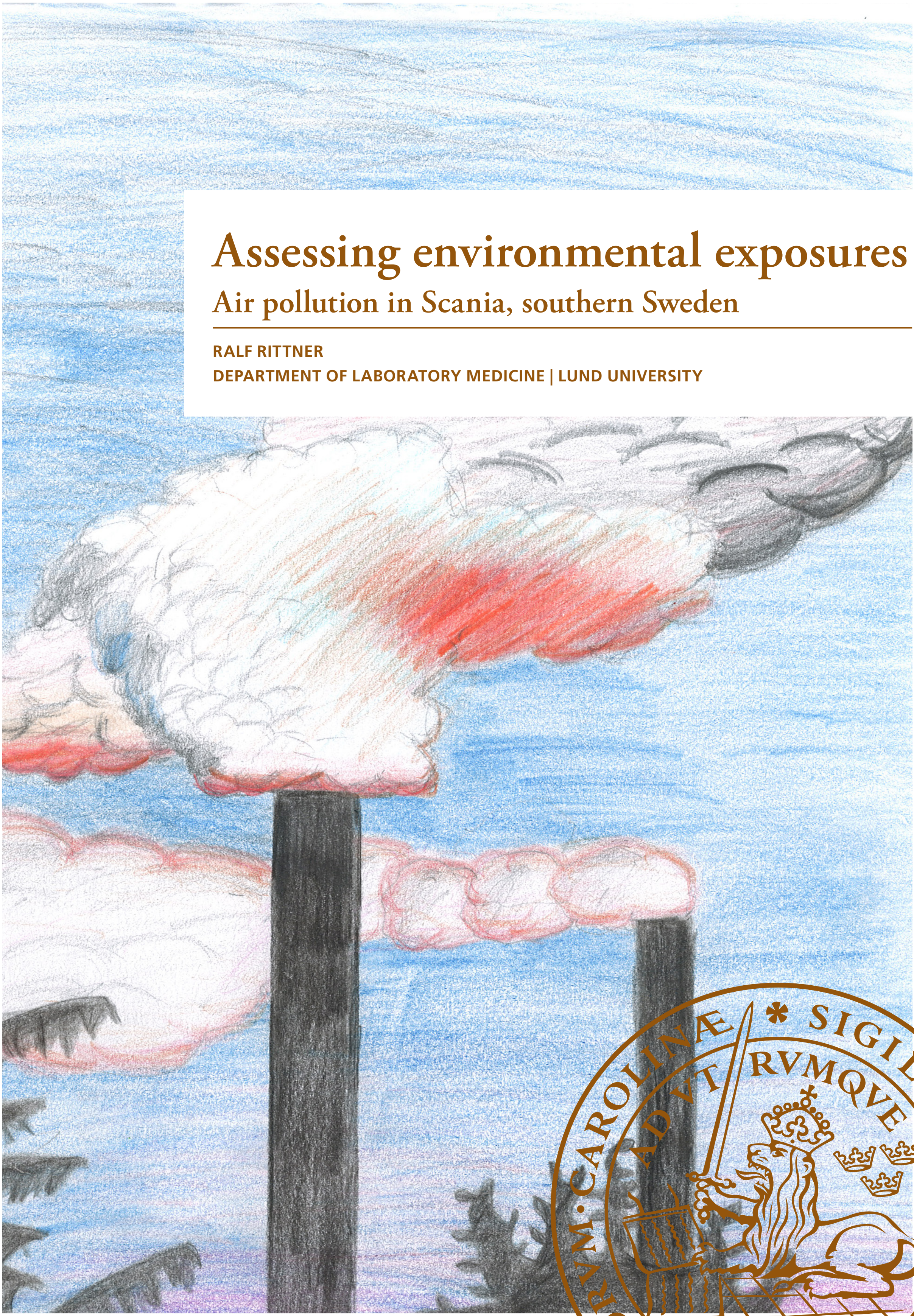

Assessing environmental exposures

Air pollution in Scania, southern Sweden

RALF RITTNER

DEPARTMENT OF LABORATORY MEDICINE | LUND UNIVERSITY

Assessing environmental exposures

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Air pollution in Scania, southern Sweden

Ralf Rittner

LUND UNIVERSITY

DOCTORAL DISSERTATION

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Air pollution in Scania, southern Sweden

Abstract

Background: The environment where we humans live provides the fundamental requirements we need to survive – food to eat, water to drink, and air to breathe. The quality of these elements has a major impact on human health, as they can contain substances that are detrimental to health. These we call environmental pollutants. This thesis explores the effects of exposure to air pollutants in particular. A large portion of the earth's population is exposed to high levels of air pollution, and 7 million premature deaths worldwide are estimated to be attributed to air pollution. In order to study relationships between exposure to air pollution and health outcomes and to quantify associations, epidemiologic research is needed. From these, exposure-response functions, or in this case air pollution concentration-response functions, are established for diseases and mortality, which form a foundation for quantitative health impact assessments (HIA). HIAs then help stakeholders and the public understand health risks and make, broadly accepted, informed decisions about interventions needed to improve public health.

Aim: To explore and evaluate methods to assess air pollution exposure in Scania for application in epidemiologic studies as well as health impact assessments.

Methods: Using a detailed emission database covering Scania, dispersion modelling of concentrations of particles and nitrogen oxides was conducted at high temporal and spatial resolutions. Modelled concentrations were evaluated against measurements (Papers I and II) and subsequently used as exposure indicators in a health impact assessment (Paper III) on premature mortality, asthma, dementia, autism spectrum disorders, preeclampsia (PE) and low birth weight. The last paper included (Paper IV) is an epidemiological study on air pollution and preeclampsia.

Results: Modelling of nitrogen dioxide (NO_2) showed a correlation of $R_S = 0.8$ with measurements at residence facades with a mean difference of 1.08 $\mu g/m^3$. Results were poorer for modelled versus measured personal exposure. Efforts to compensate for time spent at workplace did not improve the results much. Modelling of particle concentrations also showed correlations with monitor measurements. However, a large proportion of particle concentrations in Scania consists of long-range background emissions, which likely results in a high correlation between different monitors themselves, which likely contributes to the high correlation with modelled concentrations. With a mean population exposure to patricles with aerodynamic size of 2.5 µm or less ($PM_{2.5}$) of 11.9 $\mu g/m^3$, Scania experiences relatively low exposure levels from an international perspective. Still, we estimated 6% of premature deaths and 11% of low birth weight (LBW) births to be attributed to $PM_{2.5}$. Reaching a maximum $PM_{2.5}$ exposure of 10 $\mu g/m^3$ for all residents would reduce deaths and LBW substantially but could not be achieved only by removing local emissions of $PM_{2.5}$. Additional results include a positive association between air pollution exposure and preeclampsia among pregnant women.

Conclusions: Dispersion modelling is a useful tool for assessing outdoor concentrations of ambient air pollution. It should be noted that concentrations recorded outdoors at the residence of study persons do not equal someone's total personal exposure. Several alternative approaches exist, and future research will help demonstrate their respective strengths and weaknesses. It is likely that combined methods including remote sensing will prove favourable. Further, our results indicate substantial benefits for public health if the air pollution levels in Scania were reduced despite being comparatively low from an internal perspective..

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II. **Particle concentrations, Dispersion Modelling and Evaluation in Southern Sweden**, Ralf Rittner, Susanna Gustafsson, Mårten Spanne and Ebba Malmqvist, SN Applied Sciences (2020) 2:1013

III. **Health impacts from ambient particle exposure in Southern Sweden**, Ralf Rittner, Erin Flanagan, Anna Oudin and Ebba Malmqvist. International Journal of Environmental Research and Public Health 2020, Vol. 17, Issue 14

IV. **Maternal exposure to ambient air pollution and risk of preeclampsia: A population-based cohort study in Scania, Sweden**. Yumjirmaa Mandakh, Ralf Rittner, Erin Flanagan, Anna Oudin, Christina Isaxon, Mary Familiari, Stefan Rocco Hansson and Ebba Malmqvist. International Journal of Environmental Research and Public Health. 2020 Vol. 17 Issue 5

Abbreviations

BC	Black Carbon
BMI	Body Mass Index
DAG	Directed Acyclic Graph
ESRI	Environmental Systems Research Institute
CI	Confidence Interval
C-R	Concentration – Response function (exposure - response)
GIS	Geographic Information System
HIA	Health Impact Assessment
HIF	Health Impact Function
IARC	International Agency for Research on Cancer
LBW	Low Birth Weight (< 2500g)
LUR	Land Use Regression
m	meter
m^3	cubic meter
MAPSS	Maternal Air Pollution Southern Sweden
µg	microgram
NO	Nitrogen Monoxide
NO_X	Nitrogen Oxides
NO_2	Nitrogen Dioxide
O_3	Ozone
PE	Preeclampsia
PM	Particulate Matter
PM_{10}	Particles of aerodynamic diameter < 10 µm
$PM_{2.5}$	Particles of aerodynamic diameter < 2.5 µm
R_P	Pearson correlation
R_S	Spearman correlation
R^2	Squared R_P
REVIHAAP	Review of evidence on health aspects of air pollution
SCB	Statistics Sweden (Statistiska centralbyrån)
SO_2	Sulphur dioxide
WHO	World Health Organization

Abstract

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Introduction

The environment is what surrounds us humans, where we live and act alone or together, while working or spending leisure time. It can be the wild created by nature itself as well as the urban and rural landscapes formed by human hands. Our environment influences our life through impressions we see, hear and feel, but also provides us with the fundamental requirements we need to survive - food to eat, water to drink and, not least, air to breathe. Their quality can undoubtedly have a major impact on our health and wellbeing.

Indeed, all of these elements can contain substances that are detrimental to our health, i.e. environmental pollutants. Exposure to such substances can occur through uptake via the gastrointestinal tract, through dermal absorption via the skin or by inhalation via the airways.

This thesis focuses specifically on air and some of its environmental pollutants. Meriam-Webster defines the air itself as a mixture of odourless and tasteless gases, mainly nitrogen and oxygen, that surrounds the planet earth [1]. The air takes up pollutants from natural processes as well as from human activity, called anthropogenic sources, and can transport them long distances. Air pollution is not only a problem outdoors, as a result of combustion in for example vehicle engines, but also exists indoors in many parts of the world. The main sources for indoor air pollution are stoves for food preparation and heating.

Being carried by the air we breathe both outside and inside, air pollutants affect people around the world. According to the World Health Organisation (WHO), 9 out of 10 people worldwide breathe highly polluted air [2]. Their data further indicates that 7 million premature deaths every year are caused by air pollution, illustrated in Figure 1 [2].

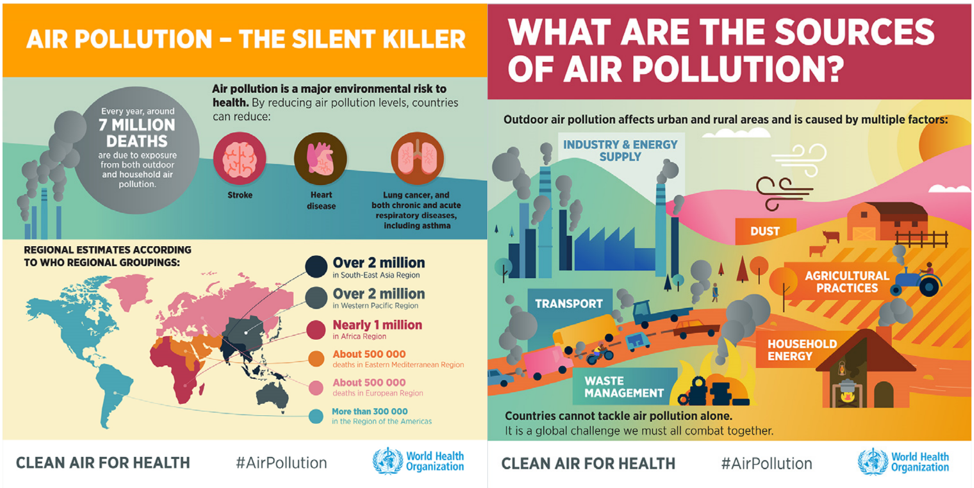

Figure 1. Infographs from WHO, from their series to raise awareness.
These chosen to illustrate burden and origin of air pollution. A number of graphs are presented and are available for downloading and sharing on social media.

The WHO presents an illustrative overview of outdoor air pollution in a fact sheet: Ambient (Outdoor) Air Pollution (visited June 4th 2020) [3]. Much attention is given to particles (particulate matter, PM), which are categorized by their aerodynamic size as illustrated in Brook et al. in their Figure 1 [4].

Most commonly mentioned are particles with a diameter of 2.5 µm or less and of 10 µm and less ($PM_{2.5}$ and PM_{10}, respectively). Studies of different particle sizes are needed since their size determines how far they are deposited in the human body. Coarser PM remain in the airways and lungs while finer particles travel further in the lungs and can even penetrate the blood-air barrier of the alveoli and thereby enter the blood system [5]. Other than size, the unique chemical composition of particles can also have consequences for human health and needs to be investigated.

In a technical report from the *Review of evidence on health aspects of air pollution* (REVIHAAP) project, the adverse health effects from air pollution are thoroughly described in a series of questions posed by the European Commission [6]. These ranged from respiratory illnesses to cardiovascular disease and even mental disorders. Further, a working group within the International Association for Research on Cancer (IARC) unanimously classified outdoor air pollution and PM as carcinogenic to humans (IARC category 1) in 2013 [7]. They stated that remarkable consistencies were found in in epidemiological research, animal studies and studies on mechanisms regarding the carcinogenicity of air pollution overall and particulate matter specifically. This conclusion was based on several large studies, some of which were restricted to nonsmokers and most of which were performed in areas with an annual mean of $PM_{2.5}$ concentrations ranging from 10 to 30 $\mu g/m^3$.

Another WHO fact sheet summarizes household air pollution and health [8] and states that 3.8 million premature deaths each year are attributable to indoor air pollution. The reason for this is stated to be that 3 billion people still cook using solid fuels such as wood, crop wastes, charcoal, coal and dung, which produce particulate as well as gaseous pollutants during combustion. Oftentimes these people lack the economic ability to replace stoves or heating equipment with more fuel-efficient and cleaner technologies e.g. electric appliances and can be unaware of the health risks associated with indoor combustion.

Comprehensive burden of disease reports are provided regularly by the WHO, which relate diseases to their various causes including environmental exposures. More and more, air pollution is being explored in connection to these reports, and as mentioned above, associations between air pollution and adverse health outcomes have been clearly documented. Still, continued research is needed in order to establish and ascertain what is called the exposure-response function, or the relationship between the level of exposure and different outcomes, such as specific diseases or mortality rate. Since the included papers investigate pollutant concentrations, we prefer the phrase concentration-response (C-R) function instead. The C-R is often expressed as the change in risk of the studied outcome in relation to a change in the exposure.

When associations are established and the size of C-R is reliable, this information can be used to estimate the burden of disease, i.e. to determine the number of cases that can be attributed to a certain exposure. Further, such research products form the foundation for HIA. A HIA involves conceiving, planning, predicting and evaluating how an intervention aimed to reduce a particular exposure will impact a population's health and wellbeing. In order for stakeholders and decision makers to communicate intentions, gain support for their initiatives and policies and participation, quantitative HIA calculations based upon epidemiologic knowledge are crucial.

Aim

Overall aim

The overall aims of this thesis are 1) to investigate possible methods to assess environmental exposures for the application in epidemiological studies as well as health impact assessments and 2) to explore means to evaluate these methods. The focus will be on air pollution in Scania, the southernmost county of Sweden.

Specific aims

Paper I

This study applies a dispersion model for NO_2 based on an emissions database to evaluate 1) how accurately ambient air pollution levels are modelled and 2) how well measured and modelled weekly residential outdoor levels correlated with personally measured exposure during a corresponding period. Further, we investigated if it is possible to improve the assessment of personal exposure by combining outdoor levels of NO_2 at home residence with those at the workplace.

Paper II

The objectives of this study are, firstly, to model concentrations of PM_{10}, $PM_{2.5}$ and black carbon (BC) in the county of Scania for the period of 2000 - 2011 and, secondly, to evaluate the result. A dispersion model based on an emission inventory covering the region was applied. The spatial resolution was grids of 100 * 100 meter squares and the temporal resolution was calendar months. The evaluation of the dispersion model compared our modelled pollution levels to available measurements from monitoring stations. Moreover, our results were used as individual exposure in Paper III and IV and will also be used in future studies.

Paper III

The purpose of the study was to estimate the health impacts of long-term exposure to $PM_{2.5}$ in Scania, with special focus on premature mortality and morbidity outcomes for sensitive groups, including pregnant women and fetuses, children and the elderly. This study expands upon previous research [9], which was limited to the city of Malmö and investigated vehicle exhaust only. Air pollution from a variety of sources are studied, and we aimed to estimate exposure and health impact for both the total air pollution content as well as for specific sources, such as local traffic and small-scale heating, to provide detailed input for policy actions.

Paper IV

The objective of this study was to further study the possible association between exposure to PM_{10}, $PM_{2.5}$ and black carbon (BC) and the risk of developing preeclampsia in a low-exposure setting using high spatial resolution PM models. Several epidemiological studies have reported a positive association between PE and maternal exposure to gaseous air pollution components, such as ozone (O_3), NO_2, and sulfur dioxide (SO_2) in both relatively low and high exposed areas [10-15]. Additionally, maternal exposure to PM_{10} as well as $PM_{2.5}$ during pregnancy has been found to be positively associated with higher risk for PE [10, 15-17]. However, some studies have found no such associations [18-20].

Material and methods

Study area and population

All studies in this thesis were conducted in Scania, which is the southernmost county of Sweden. It is situated near the European continent and is especially close to Denmark and the Danish capital, Copenhagen. Scania's geographic location is shown in Figure 2.

Figure 2. Geographic location of Scania.
Figrure by Emilie Stroh

Scania has no high mountains, only a few ridges running from south-east towards north-west, and its highest point is 212 m above sea-level [21]. According to Statistics Sweden , the population was 1.13 million in 2000, 1.24 million in 2010 and 1.38 million in 2019 and is predicted to continue to grow in the next 10 years [22].

Regarding study population, we chose appropriate groups of participants from the Scanian population based on their relevance to each specific study's research question. When exploring the possibility to assess personal exposure by modelled concentrations at certain geographical locations (Paper I), the number of participants had to be chosen according to available equipment needed for the measurements. As Paper II consisted of dispersion modelling and an evaluation of this modelling, no human study population was necessary. For the health impact study (Paper III), register data was used but in aggregated form; this enabled us to determine individual baseline probabilities for the risk of the studied outcomes with respect to age and sex. In the preeclampsia study (Paper IV), register data was also utilized, and all births occurring within the study period with complete data were included.

Exposure substances

In the enclosed papers we were interested in the population participants' exposure to air pollution. The particular pollutants included mainly nitrogen oxides NO_X and NO_2 in Paper I, $PM_{2.5}$ in Papers II and III and PM_{10}, $PM_{2.5}$, BC as well as NO_2 in Paper IV.

PM is a complex mixture of suspended solid and liquid substances in the air. Its major components consist of sulphate, nitrates, ammonia, sodium chloride, black carbon mineral dust and water. These originate from numerous sources such as combustion in vehicle engines, power production as well as other industrial processes e. g. metal smelting and other processing. Tyre and road wear, agriculture related activities, wood burning, and natural phenomena are other sources of PM [4]

NO_2 is toxic at concentrations exceeding 200 μg/m^3 and causes significant inflammation of the airways at short-term exposure. Long-term exposure at levels seen in cities has been associated with increase of symptoms of bronchitis and childhood asthma. NO_2 is also the main source of nitrate aerosols which are an important fraction of $PM_{2.5}$. Anthropogenic emissions of NO_2 are mainly due to combustion processes for heating, power generation and the operation of combustion engines in vehicles and ships [3].NO_X denotes the various compounds formed of nitrogen and oxide, such as nitrogen monoxide, NO_2, nitrogen trioxide etc, collectively. All those share the family of sources mentioned for NO_2 [4].

BC being a component of PM has been proposed to be an additional indicator for health risks related to air pollution [23]. The idea is that BC would be closer correlated to (possibly incomplete) combustion than just the size related PM fractions that are subject for regulations.

Collecting exposure data

As illustrated in Paper I, a possible exposure assessment method is to equip study participants with personal monitoring devices in order to obtain data on their individual air pollution exposure. While this may provide a more detailed and accurate exposure assessment, scaling up such an approach to studies with larger numbers of participants, requires increasingly greater resources and effort. This is attributed to both the substantial number of monitoring devices needed and also the increased collection, cleaning and management of the measurements for each study person. Another limitation is that personal monitoring does not provide the possibility to perform studies retrospectively, i.e. to obtain data about historical exposure. These opportunities and obstacles have been weighed by air pollution researchers and dealt with in various ways. As is the current standard in air pollution epidemiology, rather an assessment of a proxy for one's personal exposure is conducted instead of using personal measurements. In our case, we have relied on dispersion modelling as such a proxy.

Modelling concentrations for exposure assessment

An emission database, covering Scania, was created by and maintained through a collaboration between the Centre for Geographical Information Systems (GIS Centre) at Lund University and the Environmental Department at the City of Malmö. Parts of the continuous updating is also funded by Skånes Luftvårdsförbund, a union of organizations and companies with interest in maintaining good air quality in Scania. Initially the database and software was installed at several locations including GIS centre and Occupational and Environmental Medicine at Lund University, but lately it is kept at the Environmental Department of the City of Malmö.

Emission sources are described in detail- primarily by their geographical location and their form, including point, line or grid sources. The latter incorporates geographic distribution according to a given weighting factor, such as population density in each cell. Additionally, a number of characteristics are entered in the definition of the sources. A smokestack (chimney), for instance, has physical attributes like height, width of the outlet as well as temperature and speed of the gas flow. Sources can be described by annual emission, annual fuel consumption or by combustion effect. Traffic emissions are described using line sources that represent road segments. These can have a number of attributes, including basic data on a road's location, length and direction as well as more nuanced information on the composition of vehicle types, traffic intensity, speed limits and critical flows for congestion. In the database, vehicle types themselves can also be classified according their fuel type and emission of air pollutants at different driving conditions. Further, various time profiles can be defined at the hourly (over the day) and monthly (over the year) levels. Appropriate time profile can be assigned for each source.

The software package (ENVIMAN) used for the management and maintenance of this emission database is modular. Originally intended for air quality planning, one specific module (AQPlanner) is an implementation of a model for dispersion simulations. It is based on the reference model AERMOD from the Unites States Environmental Protection Agency, which applies a Gaussian simulation technique. In this implementation, however, the model is flat and does not take topography into consideration. Moreover, this implementation only allows for one set of meteorological parameters for each simulation run, such as an actual time series of measurements, a hypothetical setting or a climatological representation of a typical time period.

A modelling run always results in a geographical grid with concentration values of the modelled substance over the chosen area. The results can be presented in a variety of ways, including as period mean or percentiles. It is also possible to specify a list of points of interest (receptor points) and, in that case, to present modelled values only at those points. When scaling up to larger spatial areas and time periods, as in Papers II – IV as well as several other analyses performed by our department, we could take advantage of intermediate result files from AQPlanner. These contain hourly values, which we could aggregate to a mean over any desired time period. Next, the means were imported into a GIS program, we used ArcGis 10.3, and rasters covering Scania were created. The use of GIS facilitated the process by efficiently letting us extract concentration values at the coordinates of each study person's home residence, when known, for our entire study population at once.

Data linkage

In Sweden, several registers are kept for statistical purposes by different agencies and administrative offices. Statistics Sweden (SCB), for example, can provide information on residents' addresses as well as socio-economic variables such as income and education levels, among others. Health data registers, such as the medical birth register used in Paper IV, are kept by the National Board of Health and Welfare (Socialstyrelsen). This data should be used for research purposes; however, registries' differing routines for granting access can be complex. Despite this, every resident's personal identification number, introduced in 1947, is the same for all registries in Sweden and makes it possible to link data from different sources consistently and with a high grade of correctness. For privacy reasons, the registries often require researchers to first collect exposure and background data to which the registry data will be connected. The key, which enables the requested socio-economic or health data to be linked to a certain individual, is kept secure by the registry. Figure 3 shows a schematic of the process of linking exposure, outcome and covariate data.

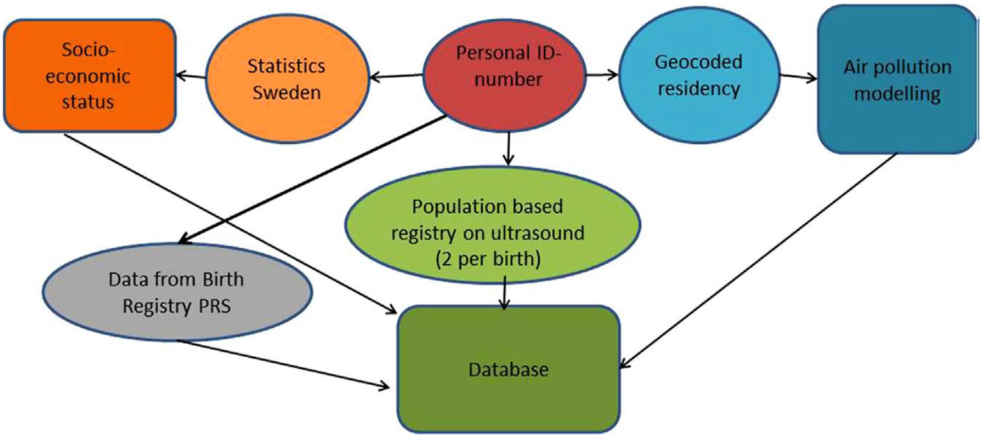

Figure 3. Schematic view of data collection. From Malmqvist et al. [24]

Variables of interest

In addition to exposure data we needed outcome variables for Papers III and IV. They are as listed below.

Paper III

For this study, a quantitative health impact assessment study bordering a burden of disease estimation, we selected several health outcomes: asthma, preeclampsia, dementia, LBW and mortality. While quite diverse, these were consciously chosen in order to demonstrate the range of impacts air pollution has on human health [25, 26].

LBW is not a disease per se but rather a risk factor for health complications later in life [27-30]. In this paper, calculations were based on the incidence of the aforementioned health outcomes combined with established exposure risk estimates. Because of this, no confounding factors needed to be included as is typically required in epidemiological analyses.

Paper IV

This paper's sole outcome of interest was preeclampsia, including both moderate and severe PE. The source was the local database MAPSS (Maternal Air Pollution Southern Sweden), which was built from a local high-quality birth register combined with individual air pollution levels as well as socioeconomic and sociodemographic information from Statistics Sweden. MAPSS is further described by Malmqvist et al. [24]. As this was an epidemiological association study, obstetrical risk factors and other confounders needed to be accounted for. All such data was also available in MAPSS. Directed acyclic graphs (DAG) [31], which allow for analysing the causal pathway from exposure to outcome graphically, were used to help select variables to control for in statistical modelling. The included intermediate and confounding factors can be seen in Paper IV, and the DAG used to derive them are presented in the supplementary material for this paper.

Statistical methods

Comparison of measured and modelled concentrations

Bland-Altman diagrams are a tool for graphically analysing the relation between a *gold standard* and a new method. In Paper I, the measurements performed were used as the gold standard and our dispersion modelling results as the examined method, see Figure 4 for an illustration. The difference between the two is plotted against the gold standard value on the x-axis [32]. With ideal, perfect consistency, all points would line up on the y-axis zero.

Further, Spearman correlation coefficients and linear regression were also to utilized for the evaluation comparisons.

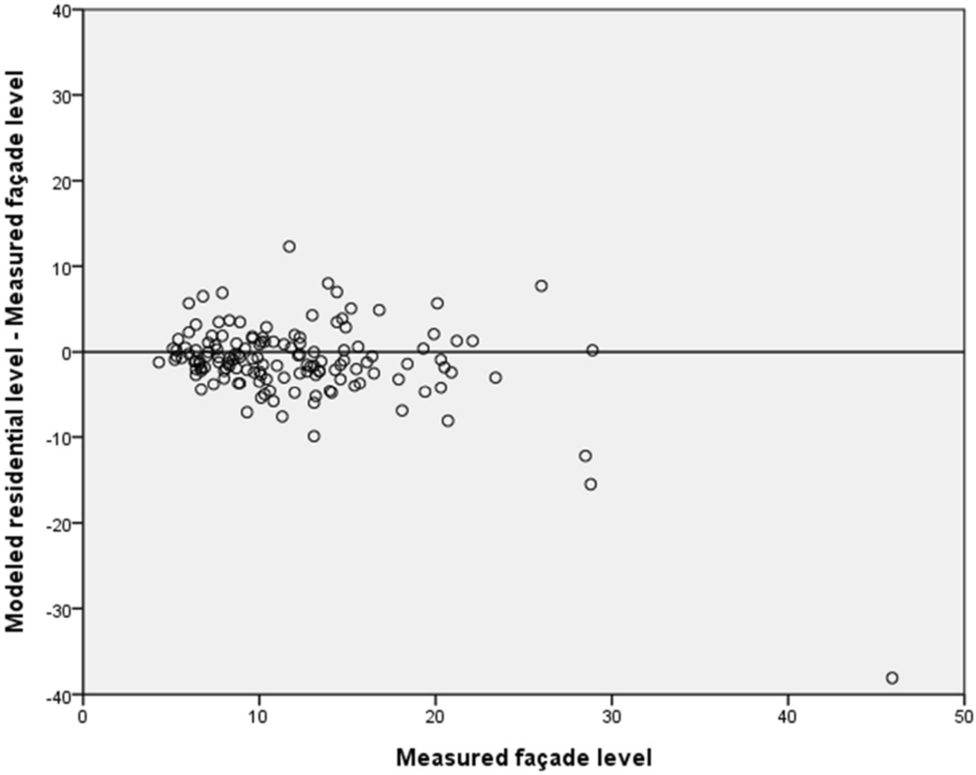

Figure 4. Illustration of Bland-Altman diagram. From Paper I.
The difference between modelled and measured values against measured NO_X concentrations on the x-axis (unit: µg/m^3).

An additional measure of comparison used in Paper II was Pearson correlation coefficient, which was calculated to maintain consistency with a prior report for the Swedish Environment Protection Agency (Naturvårdsverket) [33]. We incorporated mean bias expressed as the mean of differences between measured and modelled concentrations. The root mean squared error was also calculated in this paper.

Health impact analyses

We used a health impact function (HIF) described by the following formula:

$$\Delta Y = Y_0 * (1 - e^{-\beta * \Delta x})$$

Here, ΔY is the change in the outcome of interest, Y_0 is the baseline incidence for the outcome (we used the probability for each study person), β is the C-R function, and

Δx is the change in exposure. This formula is based on a log-linear risk coefficient. The calculation was performed for each individual in the actual population with Δx being a hypothetical reduction of their known individual air pollution exposure. The resulting individual ΔY's were summed to provide the total change in health outcome case numbers. Since the exposure was known for each study person Y_0 should not be multiplied by a factor for probability of exposure. As Martennies et al. [34] mention, the HIF represents a simplified form of the population attributable fraction. By inserting a population's entire exposure as Δx, one can calculate the burden of disease for that exposure. This can also be interpreted as the hypothetical scenario of removing the exposure altogether. We continued to study different scenarios, as described in Paper III, by subtracting certain target level from modelled personal exposure concentrations. The remainder which would be the hypothetical exposure reduction was then used as Δx. For example, the WHO proposes an annual maximum mean $PM_{2.5}$ concentration of 10 µg/m^3 [35].

The birth cohort

Binary logistic models were applied to analyses in Paper IV. A complete case analysis leaving out cases with missing data was the main model. The pollutants under investigation (PM_{10}, $PM_{2.5}$ and BC) had to be analysed separately due to the high correlation between them, especially locally produced emissions. These exposures were treated as both continuous variables with increments of 1 or 5 µg/m^3 for BC and PM, respectively, as well as categorical divided into quartiles. The whole pregnancy period as well as individual trimesters were analysed.

Software

Throughout the PhD project period, different versions of IBM SPSS Statistics have been available and utilized for the completed papers. R was also used to write original scripts for various data management tasks. ArcGis from Environmental Systems Research Institute (ESRI) was used for similar purposes, and the most current at the time of use was always employed.

Results and comments

Paper I

In Paper I, which concentrated on NO_2, strong correlations were observed between our dispersion modelling results and measurements made at the facades of the study persons' residences. Statistical analysis showed a Spearman correlation (R_S) of 0.8 and the mean difference to be 1.08 μg/m^3 (paired t-test with 95% CI = 0.28 – 1.88 μg/m^3). In comparison to measured personal exposure, the modelling results correlated more poorly with an R_S of 0.4. The correlation did not improve much by attempting to compensate for time spent at work by combining outdoor concentrations at the residence with those at the workplace when it was known for study persons. In these comparisons, the modelled levels tended to underestimate the true measured levels at lower NO_2 concentrations and overestimate measured levels at higher NO_2 concentrations.

Paper II

For Paper II, the emission database was supplemented with emission factors for particles (PM_{10}, $PM_{2.5}$ and BC). These were used to build a set of rasters with high spatial resolution (100 m * 100 m). The temporal resolution was aggregated from its original hourly mean values to monthly averages because knowledge acquired from the previous work (Paper I) cautioned against studying short-term exposures based on this dispersion modelling. The original data files from the dispersion modelling software are saved and stored, which allows for temporal divisions or aggregations according to the appropriateness for a particular research question, method, study setting or study population. The evaluation of this large data set which was produced in a retrospective way could for obvious reason not be performed against measurements planned and performed before the modelling. Instead, we had to collect as much data as possible from air quality monitoring stations in Scania that had been operating during the study period. We located seven such monitors. The subsequent evaluation of our modelled PM against measured levels showed R^2-values from 0.46 to 0.83 for $PM_{2.5}$ and, similarly, 0.44 to 0.86 for PM_{10}. Too few BC measurement series were identified during the project timeframe, resulting in the inability to evaluate this substance and to identify background levels of BC derived from long-range transport by air. See Table 2 in Paper II for typical concentrations of PM modelled at each monitoring station's geographical location and Table 3 for their evaluation results. Additionally, we later investigated the correlations between the monitor measurements series from the 7 monitoring stations (see Table 1 below). The implications of these results are further elaborated upon in the General discussion section.

Table 1. Pearson correlations between monitor measurements used in Paper II.

	Malmö D.		Trelleborg		Kristian-stad		Lands-krona		Lund		Hässleholm		Burlöv	
	$PM_{2.5}$	PM_{10}	$PM_{2.5}$	PM_{10}	$PM_{2.5}$	PM_{10}	$PM_{2.5}$	PM_{10}	$PM_{2.5}$	PM_{10}	$PM_{2.5}$	PM_{10}	$PM_{2.5}$	PM_{10}
Malmö Dalaplan	1.0	1.0												
Trelleborg	0.7	0.9	1.0	1.0										
Kristian-stad				0.7		1.0								
Lands-krona	0.8	0.8	0.8	0.9		0.8	1.0	1.0						
Lund		0.8		0.8		0.7		0.8		1.0				
Hässle-holm		0.8		0.9		0.8		0.9		0.9		1.0		
Burlöv		0.9		0.9		0.7		0.7		0.9		[a]		1.0

[a] Measurement series not overlaping.

Paper III

The $PM_{2.5}$ concentrations derived from the previous paper (Paper II) then constituted the base for exposure in our health impact assessments. We used the concentrations modelled for the year 2011, which was the last year in the data set and could be considered a typical meteorological year. Overall, the Scanian population was exposed to an annual mean outdoor $PM_{2.5}$ concentration of 11.88 µg/m^3 with the population mean exposure ranging between 9.56 and 19.4 µg/m^3. Of the total annual mean exposure, local sources of $PM_{2.5}$ contributed to only 0.88 µg/m^3 (7.4%). In comparison, the annual population mean exposure to $PM_{2.5}$ in Stockholm, the capital of Sweden, was found to be 6.5 µg/m^3; however, the locally produced $PM_{2.5}$ constituted a larger proportion of the total at 1.9 µg/m^3 (29%) [36]. With this, we found that Sweden and our study setting of Scania had relatively low population exposure to $PM_{2.5}$ comparted to exposure levels internationally.

When applying our modelled exposure concentrations to the Scanian population for the year 2016, we estimated 6% of premature deaths and 11% of LBW births to be attributed to the total concentrations of $PM_{2.5}$ outside residents' homes. According to our estimations, a reduction of $PM_{2.5}$ to a maximum annual mean concentration of 10 $\mu g/m^3$ for each person, would substantially reduce premature deaths (294 out of 10,987 cases) and LBW (15 out of 757 cases). To achieve this air quality guideline, which is recommended by the WHO, it would, in most cases, not suffice to only eliminate all locally produced and emitted $PM_{2.5}$.

Paper IV

In Paper IV, 1,034 occurrences (2.9%) of PE out of the 35,570 births were studied. The development of PE was more common among women with certain characteristics, such as high body mass index (BMI), gestational diabetes, hypertension as well as having a male child and experiencing their first birth, see Table 1 in Paper IV. Nordic-born women had a higher proportion of PE cases, and PE was less common among smokers. Regarding exposure, younger women and women having lower SES (i.e. low educational attainment, foreign country of birth and low income) were more likely to experience higher levels of air pollution at their residence. When estimating the effects of air pollution expressed as odds ratios for highest quartile of exposure relative to the lowest, all studied pollutants showed significant effects for the entire pregnancy (Table 3 in Paper IV). Furthermore, local particles and NO_X also demonstrated significant effects for all pregnancy trimesters, see Table 3 in Paper IV. NO_X in particular showed the largest effects at nearly every exposure window, with the only exception being the 2nd trimester where BC had a slightly higher effect. However, when analysed without intermediate variables (gestational diabetes, gestational hypertension, and essential hypertension), the effects of NO_X and BC became similar in the 2nd trimester. Logistic regression analyses investigating incremental increases of PM (1 $\mu g/m^3$ for BC and 5 $\mu g/m^3$ for $PM_{2.5}$ and $PM_{2.5}$) resulted in a similar pattern with the highest odds ratios being for local $PM_{2.5}$ over the entire pregnancy: 2.74 (95% CI 1.69 - 4.44), followed by 2.09 (95% CI 1.42 – 3.08) for the 2nd trimester. These results are shown in the supplementary material of Paper IV. The odds ratios estimated for total $PM_{2.5}$ and total PM_{10} concentrations had consistently lower statistical significance (p-values over 0.01) at the trimester level.

General discussion

Using modelled air pollution concentrations to assess exposure in epidemiological studies and health impact assessments is a well-established method [37-40]. Modelling has been shown to be useful to assess outdoor concentrations of both gases such as NO_X, which can be recalculated to NO_2, and particles including PM_{10} and $PM_{2.5}$. As discussed in detail in Paper I, these modelled concentrations can differ substantially from measured personal exposure, which must be considered when interpreting results.

In this thesis we have used a flat dispersion model implementation based on AERMOD, which is a Gaussian dispersion model. Several other approaches exist including puff models, such as CALPUFF [41], and Eulerian models [42, 43]. Land use regression (LUR) introduced by Briggs et al. [44], which is the fitting of a statistical model to a set of variables in order to predict pollution levels, is another widely used method for modelling air pollution concentrations. When starting a new project, it might be more efficient to perform a limited number of necessary measurements and build a statistical model that can be based on a small set of predictive variables, as opposed to building an entire emission database from scratch.

For LUR modelling of ozone over two Swedish cities, Umeå and Malmö, Malmqvist et al. used four variables that were picked from urban green area, natural area, traffic density and population density determined by varying buffer sizes [45]. They found an R^2 of 0.4 in leave-on-out cross validation for Malmö, the largest city in Scania. In comparison, the R^2 values found in Paper II for dispersion modelling throughout Scania as a whole ranged from 0.44 – 0.86 for $PM_{2.5}$ and 0.46 – 0.83 for PM_{10}, with the highest values obtained in and close to Malmö.

Comparing average Pearson R_P correlations for dispersion modelling and LUR, de Hoogh et al. state that results from these two methods typically correlated well with measured NO_2 (R = 0.74) but only moderately for PM_{10} and $PM_{2.5}$ (R = 0.58) [46]. Recently, machine learning methods, such as random forest, are being utilized for modelling air pollution with promising results, especially to cover larger geographical areas [47-49]. Combinations of LUR and chemical transport models are also being presented, which now have the possibility to incorporate remote sensing data from satellite images [50, 51].

These other methods often utilize a coarser spatial resolution of 1 km * 1 km or, when using higher resolution, are limited to a smaller spatial area, often an urban area. Our studies in this thesis were based on mainly on 100 m * 100 m grids. Only in earlier works (Paper I) when modelling NO_X/NO_2, was a coarser resolution of 500 m * 500 m used. This resolution might be more appropriate for rural areas than urban ones, and while Scania is largely rural, exposure may have been underestimated in the region's many cities. Still, those dispersion modelling results have been successfully applied in several studies published from our department [9, 11, 24, 52, 53].

Since our PM dispersion model evaluation was conducted (Paper II), we have come to recognize that the majority of PM present in Scania are long-range, in-transported background particles. This fact is further elaborated upon in Paper III. Because of this, the measurements from the monitors situated throughout Scania, which were used for our evaluation, were found to be highly correlated with one another (see Table 1). Therefore, we will need to be more careful when assessing the correctness of such modelling results in the future.

A main limitation in the modelling results throughout the presented papers was that we were only able to use one set of meteorological parameters in each run. However, we have consistently used actual measured weather since we are interested in linking one's exposure to specific periods in time, such as a woman's pregnancy period, when a health complication or disease develops, or even a death occurs. Some reports concerning air quality are instead based on a set of typical weather conditions and can only yield annual mean values of pollutant concentrations. Running models with actual weather data, on the other hand, makes it possible to have access to hourly values, which gives researchers the flexibility to freely choose their resolution for temporal aggregation.

We acknowledge that we are working over quite a large spatial area, and this expansive study setting could partially explain why our dispersion model did not function uniformly across Scania. Indeed, the best performance could be seen in the southwest corner of the county. This could have a number of explanations. To begin, that area, which includes the city of Malmö, is both the most densely populated part of the county and also where the emission database has the highest precision. Further, the meteorological monitor used in the dispersion simulations is located in Malmö, which yields the highest correlation with actual weather conditions in the surrounding area.

As elaborated in Paper I, it is important to communicate and, when interpreting results, to consider that modelled exposure is always an approximation of what measurements would yield at a location. To an even larger extent, modelled exposure approximates a study person's total individual exposure. With this, a great number of possible exposure misclassification sources exist. For instance, people spend their time very differently and, largely, at different places away from their homes, such as their workplace, schools or leisure activities. It is also difficult to control for how persons transport themselves and how much exposure they experience in the process, especially in large register-based studies. Only in recent years have the Swedish population registers expanded to include information on apartment location within the building (i.e. floor number). We have traditionally modelled concentrations for 2 m above ground, leaving the possibility of exposure misclassification for those in tall apartment buildings. Another aspect that is difficult to account for is how the population airs their homes including the direction which opened windows face. Additionally, some people own fireplaces or other wood-burning stoves, and the extent of their leisure use at home could add to one's personal exposure. Residential movement might also be a source of exposure misclassification when using home address at the start of the study period as the point to determine air pollution concentration to be the designated exposure value. While investigating this misclassification source, Oudin et al. found that adults tended to have similar exposure levels after moving to a new address [54]. For others, however, changes of address could be related to health conditions as elderly needing to move to care centres situated in more central (possibly more polluted) locations, due to physical or mental conditions.

In general, non-differential exposure misclassification tends to attenuate studied associations, while the impact of differential misclassification, where the degree of misclassification depends on the study person experiencing the health issue studied, or not, is more unpredictable. The studies included in this thesis on HIA (Paper III) and PE (Paper IV) were based on all relevant, available population data. We, therefore, do not consider exposure misclassification to have been differential with regard to the studied health outcomes.

Scania being close to its neighbouring countries of Poland, the Baltic states and even Germany results in the county being influenced by air pollution emissions in these countries. Unfortunately, those sources are difficult to incorporate into the emission database and, consequently, into the dispersion calculation. In Paper III we established that of the Scanian population's average annual $PM_{2.5}$ exposure of 11.88 $\mu g/m^3$, only 0.88 $\mu g/m^3$ originated from local sources (i.e. sources contained in the emission database). These numbers clearly demonstrate the need to assess long-range transported pollutions, also commonly referred to as background levels, in exposure assessments. Despite the large extent of background levels, we were still able to demonstrate health impacts from locally emitted $PM_{2.5}$ in Paper III. In order to achieve even greater public health improvements, however, the reduction of local emissions, which would be easiest for local decision makers to manage, would be needed to be accompanied by action on an international level.

For the quantitative health impacts calculations (Paper III), the intent was to apply C-R functions from previous epidemiological research reviewed in meta-analyses to ensure they were based on as much evidence as possible. Malmqvist et al. previously illustrated the dramatic effect of using different C-Rs; in one case, the number of attributed deaths almost doubled [55]. Still, we were forced to rely on single studies for some health outcomes, including dementia and autism spectrum disorders. This indicates the need for further research in order to better ascertain the risks attributed to a particular exposure.

In Paper IV we demonstrate a significant association for the risk of developing preeclampsia and exposure to air pollution, which is in line with other [16, 17, 56] findings. The physiological effects and toxicity of air pollutants in relation to preeclampsia are more in the scope of the main author's project rather than in the scope of this thesis. Even so, Paper IV still connects and relates to this thesis as a whole: for instance, its exposure assessment is based on Paper II and is similar to what was applied in Paper III. Its strengths include the large cohort and the high-resolution dispersion modelling based on the detailed emission database. Additionally, using the exact geographical coordinates of women's residences from a reliable source and using one's Swedish pin number to link predictor variables from MAPSS and socioeconomic covariates from Statistics Sweden are both clear strengths. Still, the limitation of exposure misclassification, was present because, as discussed previously, occupational exposure, exposure during commuting and the women's indoor air pollution exposure could not be controlled for. The lack of data on PE diagnosis date made assessments of precise exposure duration during the pregnancies unfeasible. Further, the complete case analysis performed, which excluded women with lacking data on covariates, is known to be a possible source of bias away from the null.

Conclusions

Using dispersion modelling based upon a high-resolution emissions database was found useful for estimating outdoor concentrations of particles as well as gases like NO_X, which can be a basis for NO_2 calculation. This was demonstrated in different ways, such as when modelled data was compared to results from specific measurement campaigns at test persons' home facades (Paper I) and when modelled data was evaluated against measurements from air quality monitoring stations with acceptable correlations (Paper II).

As illustrated in Paper I, however, using outdoor residence concentration values when aiming to capture the personal exposure of study participants is an imperfect method. Even so, it has thus far not been, and likely will not become, feasible to attach measuring equipment to each participant in larger study settings in order to accurately measure individual exposure. Epidemiological studies and health impact assessments, thus, have overwhelmingly relied on exposure assessments based on outdoor concentrations at the study population's residences. Using this method, they have successfully found associations between air pollution and their health outcomes of interest despite plausible exposure misclassification.

In Paper II the emission database had been expanded to include data on particle emissions. We decided to make use of that by building a dataset covering a particular timespan. With this, it would be possible to also include particle exposure in our health impact assessments and epidemiological studies, as was done in papers III and IV. The most available form of this dataset is in GIS layers of monthly averages and a spatial resolution of 100 m * 100 m. However, the raw data with an hourly time resolution has been saved, making it possible to create other aggregations if the need arises. Since the evaluation of modelled PM against actual measurements yielded promising results, our research group had confidence in continuing to use the modelled concentrations for exposure assessments in subsequent studies.

The exposures resulting from Paper II were then used in combination with epidemiological findings on the exposure-response ratios of particulate air pollution in Paper III. In doing so, we showed that $PM_{2.5}$ has substantial impacts on morbidity as well as mortality. We stated that the reduction of $PM_{2.5}$, from both locally emitted and long-range transported sources, should be prioritized by authorities on all levels because of the health benefits to be gained in the population.

Finally, in Paper IV we studied pregnant women's risk of developing preeclampsia with regard to ambient air pollution exposure. While these women's exposure levels were generally below EU air quality directives, these concentrations as population annual mean were still above WHO guidelines. Our findings were consistent with previous studies, demonstrating that air pollution exposure is an important contributing factor for the development of preeclampsia. This was yet another result stressing the need to reduce ambient air pollution, even in low-exposure areas such as Scania.

Selection of authors papers not included in this thesis

Estimated health benefits of exhaust free transport in the city of Malmö, Southern Sweden. Malmqvist E, Lisberg Jensen E Westerberg K, et al.
Environment International (2018) 118 78-85

Exposure-response relationships for work-related neck and shoulder musculoskeletal disorders - Analyses of pooled uniform data sets
Nordander C, Hansson G, Ohlsson K et al.
Applied Ergonomics (2016) 55 70-84

Road traffic noise, air pollution and myocardial infarction: a prospective cohort study. Bodin T, Björk J, Mattisson K et al.
International Archives of Occupational and Environmental Health (2016) 89(5) 793-802

Mesoamerican nephropathy: Geographical distribution and time trends of chronic kidney disease mortality between 1970 and 2012 in Costa Rica. Wesseling C, Van Wendel De Joode B, Crowe J et al.
Occupational and Environmental Medicine (2015) 72(10) 714-721

Exploring inter-rater reliability and measurement properties of environmental ratings using kappa and colocation quotients. Jonas Björk, Ralf Rittner and Ellen Cromley.
Environmental Health 13 article nr 86 (p1-11), 2014

Acute myocardial infarction detected in the 12-lead ECG by artificial neural networks. Hedén B, Öhlin H, Rittner R et al.
Circulation (1997) 96(6) 1798-1802

Populärvetenskaplig sammanfattning

Miljön som omger oss påverkar vår hälsa och vårt välbefinnande på många sätt. Den är också direkt nödvändig för vår överlevnad genom att förse oss med mat att äta, vatten att dricka och luft att andas. Samtidigt kan både marken, vattnet och luften innehålla ämnen som är skadliga för vår hälsa, såväl från naturliga källor som från mänskliga aktiviteter vilka lett till utsläpp av olika ämnen i miljön. Denna avhandling fokuserar på luften som omger oss alla och som därmed är en viktig källa till hälsoskadliga föroreningar. Enligt Världshälsoorganisationen (WHO) andas nio av tio personer på jorden kraftigt förorenad luft och sju miljoner förtida dödsfall inträffar årligen på grund av luftföroreningar. Detta är därmed ett av vår tids största miljöhälsoproblem som påverkar ett stort antal personer såväl globalt som nationellt.

Det är därför av stor vikt att studera i vilken utsträckning människor utsätts för föroreningar via luften, vilka hälsoeffekter detta ger upphov till och, inte minst, vilka vinster i form av minskad ohälsa som olika åtgärder för att minska halterna av luftföroreningar kan ge. För att kunna genomföra denna typ av studier behöver vi utveckla och utvärdera lämpliga vetenskapliga metoder.

En nyckelfaktor är att kunna fastställa exponeringen, d.v.s. vilka halter människor utsätts för av olika föroreningar. Det mest direkta sättet är naturligtvis att mäta hur mycket en enskild person exponeras för genom att utrusta enskilda individer med bärbar mätutrustning. Detta är också praktiskt möjligt och har genomförts i olika sammanhang till exempel Naturvårdsverkets miljöövervakning. Det kan dock innebära en del praktiska svårigheter i synnerhet när man vill veta exponering för stora antal individer eller göra en undersökning i efterhand. Tillgången till mätutrustning kan vara begränsad och det innebär också mycket arbete att samla in och bearbeta alla mätresultat. Det går inte heller att bestämma hur människors exponering sett ut bakåt i tiden, något som kan vara av intresse när man vill koppla exponeringen till hälsoeffekter. Ett alternativ är därför att ta fram en datormodell som kan beräkna hur människors exponering ser ut både nu och bakåt i tiden. En del av arbetet med denna avhandling har bestått i att ta fram och utvärdera en sådan modell för luftföroreningar i Skåne. Modellen bygger på att samla information så komplett information som möjligt om befintliga utsläppskällor i området man vill studera. Och sedan beräkna/simulera hur utsläppen sprids i omgivningen med hjälp av bland annat väderförhållanden. Vi har fokuserat dels på partiklar med olika storlek och dels på gaser i form av kväveoxider. Båda dessa föroreningstyper är välkända för att ge upphov till ett flertal olika hälsoeffekter hos människor. För att utvärdera hur bra modellen är på att förutsäga halter av luftföroreningar har de modellerade halterna sedan jämförts med uppmätta halter från olika mätstationer i Skåne. Resultaten visar att tillfredsställande överenstämmelse mellan modellerade och mätta utomhus halter. Vi har därmed visat att spridningsmodellering är ett användbart verktyg för att uppskatta exponeringen för ett stort antal människor över en längre tidsperiod. De modellerade halterna kan illustreras på digitala kartor och i dessa kan man lätt ”läsa av” värdet i ett stort antal punkter, t ex bostadsadresser.

När vi hittat en metod för att bestämma exponeringen är nästa steg att koppla denna till hälsoeffekter såsom insjuknanden eller förtida dödsfall, d.v.s. vilken risk har människor att drabbas av olika typer av hälsoeffekter när de utsätts för dessa halter av partiklar och kväveoxider. Detta görs genom så kallade epidemiologiska studier där man söker statistiska samband mellan graden av exponering och förekomsten av en viss hälsoeffekt inom en stor grupp människor. Uppgifter om exponeringen kan fås med hjälp av den datormodellering som beskrivs ovan och uppgifter om hälsoeffekter kan fås från olika typer av medicinska register som finns tillgängliga i Sverige.

När man med denna typ av statistiska undersökningar fastställt samband mellan en viss hälsoeffekt kan detta samband utnyttjas i så kallade hälsokonsekvens-uppskattningar. Det innebär att man tar reda på dels hur stor andel av hälsoeffekten som kan tillskrivas en nuvarande exponering dels kan beräkna en uppskattning av hur stor del av antalet insjuknanden eller dödsfall som skulle minska om en viss åtgärd som ger minskad exponering genomförs. Vi har bland annat kunnat visa att 6 % av de förtida dödsfallen i Skåne 2016 liksom 11 % av fallen där barn föddes med låg födelsevikt kan kopplas till halten av partiklar med diametern 2,5 mikrometer ($PM_{2,5}$) utanför personernas bostäder. Låg födelsevikt är inte en negativ hälsoeffekt i sig, men utgör en riskfaktor för att drabbas av andra typer hälsoeffekter senare i livet. Att vidta åtgärder för att minska halterna av luftföroreningar i Skåne skulle därmed ha stora positiva effekter för människors hälsa. Denna typ av information är mycket viktig för allmänheten men även myndigheter och beslutsfattare för att förstå och kommunicera förväntad nytta av planerade miljöförbättrande åtgärder.

Slutligen valde vi också att redovisa en epidemiologisk studie över havandeskapsförgiftning (preeklampsi PE) och olika luftföroreningar. Alla tidigare studier har inte visat entydiga resultat för PE avseende partikelexponering. Resultatet visade även här effekt av partikelexponering i Skåne redan vid de internationellt sett låga halter som finns här. Tydligast för de som tillhörde fjärdedelen med högst exponering bland de studerade gravida kvinnorna. Detta är ännu ett resultat som understryker vikten av minskade luftföroreningshalter i Skåne.

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